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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/608,066	06/30/00	ASTATKE	M 0942.4990001

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EXAMINER	
TAYLOR,J	
ART UNIT	**PAPER NUMBER**
1655	13

DATE MAILED: 10/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary	Application No. 09/608,066	Applicant(s) ASTATKE ET AL.	
	Examiner Janell Taylor Cleveland	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-29,33,34 and 60-88* is/are pending in the application.

4a) Of the above claim(s) *12-29,33,34,61-63 and 83-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The following is a FINAL REJECTION. Any rejection not reiterated is withdrawn. A Response to Arguments section follows.

Election/Restrictions

1. Newly submitted claims 12-29, 32-34, and 60-63, as well as 83-88, are directed to an invention that is independent or distinct from the invention originally claimed (which is now presented in new claims 64-80) for the following reasons: the claims have been amended to recite limitations found in those claims which were non-elected in the Response to Restriction filed January 16, 2001. Claims 12-29, 32-34, and 60-63 have been amended (or newly added) to recite that the inhibitors each comprise a 5' portion, a 3' portion, said 3' portion comprising one or more deoxyribonucleotides or derivatives thereof and said 5' portion comprising one or more ribonucleotides or derivatives thereof. Furthermore, claims 83-88 have been newly added, and these claims recite mixing one or more mRNA templates with one or more reverse transcriptases. These limitations were part of those non-elected claims, and will therefore not be examined as they are drawn to an invention which is independent and distinct from the invention originally claimed. For that reason, only claims 64-82 will be examined, as they are drawn to the same limitations as original claims 12-29 and 32-34.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 12-29, 32,34, 60-63, and 83-88 are

withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

2. Claims 64-74 are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al. (USPN 6,020,130).

Claim 64 is drawn to a method for synthesizing a nucleic acid molecule comprising: mixing at least one enzyme with polymerase activity with one or more double-stranded nucleic acid inhibitors and one or more templates; and incubating said mixture under conditions sufficient to synthesize one or more first nucleic acid molecules complementary to all or a portion of said templates. Claim 65 is drawn to the method of claim 64, wherein said mixing is accomplished under conditions to prevent nucleic acid synthesis and/or to allow binding of said nucleic acid inhibitor to said enzyme with polymerase activity. Claim 66 is drawn to the method of claim 64, wherein said synthesis is accomplished under conditions sufficient to reduce the inhibitory affect of said nucleic acid inhibitor. Claim 67 is drawn to the synthesis being accomplished in the presence of at least one component selected from nucleotides or primers. Claim 68 is drawn to the template being double stranded. Claim 69 is drawn to making second

nucleic acid molecules complementary to first nucleic acid molecules. Claim 70 is drawn to a method for amplifying a nucleic acid molecule comprising: mixing at least one double stranded nucleic acid inhibitor with one or more enzymes with polymerase activity and one or more templates; and incubating said mixture under conditions sufficient to synthesize one or more first nucleic acid molecules complementary to all or a portion of said templates. Claim 71 is drawn to the method of claim 70, wherein said mixing is accomplished under conditions to prevent nucleic acid synthesis and/or to allow binding of said nucleic acid inhibitor to said enzyme with polymerase activity. Claim 72 is drawn to the method of claim 70, wherein said synthesis is accomplished under conditions sufficient to reduce the inhibitory affect of said nucleic acid inhibitor. Claim 73 is drawn to the amplifying being accomplished in the presence of at least one component selected from nucleotides or primers. Claim 74 is drawn to the template being double stranded .

Gold et al. teach "The present invention includes methods of identifying and producing nucleic acid ligands to DNA polymerases. Specifically included are methods for identifying nucleic acid ligands to thermostable DNA polymerases useful in the Polymerase Chain Reaction, including the Taq and Tth polymerases and the nucleic acid ligands so identified and produced. More particularly, *DNA sequences are provided that are capable of binding specifically to the Taq and Tth polymerases respectively, thereby inhibiting their ability to catalyze the synthesis of DNA at ambient temperatures.* The method of this invention can be extended to identifying and producing nucleic acid ligands to any thermostable DNA polymerase and the ligands so identified and

produced." (Col. 5, line 60 through Col. 6, line 6). Gold goes on to say that included in the invention is an improved method of performing PCR (Col. 6). Therefore Gold teaches all of the limitations of claims 64-74.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al.

Claim 80 is drawn to a method for amplifying a double stranded DNA molecule, comprising providing a first and second primer, wherein said first primer is complementary to a sequence within or at or near the 3' termini of the first strand of DNA molecule and said second primer is complementary to a sequence within or at or near the 3' termini of the second strand of said DNA molecule and one or more nucleic acid inhibitors prevent or inhibit nucleic acid synthesis; hybridizing said first strand and said second primer to said second strand to form hybridized molecules; incubating said hybridized molecules under conditions sufficient to allow synthesis of a third DNA molecule complementary to all or a portion of said first strand and a fourth DNA molecule complementary to all or a portion of said second strand; denaturing and repeating one or more times. Claim 81 is drawn to a method of preparing cDNA from mRNA, comprising mixing one or more mRNA templates, one or more reverse

transcriptases, and with one or more nucleic acid inhibitors; and incubating said mixture under conditions sufficient to synthesize one or more cDNA molecules complementary to all or a portion of said templates. Claim 82 is drawn to the method of claim 81, wherein said mixing is accomplished under conditions sufficient to prevent nucleic acid synthesis and/or allow binding of said nucleic acid inhibitor to said reverse transcriptase.

Gold et al. teach "The present invention includes methods of identifying and producing nucleic acid ligands to DNA polymerases. Specifically included are methods for identifying nucleic acid ligands to thermostable DNA polymerases useful in the Polymerase Chain Reaction, including the Taq and Tth polymerases and the nucleic acid ligands so identified and produced. More particularly, *DNA sequences are provided that are capable of binding specifically to the Taq and Tth polymerases respectively, thereby inhibiting their ability to catalyze the synthesis of DNA at ambient temperatures.* The method of this invention can be extended to identifying and producing nucleic acid ligands to any thermostable DNA polymerase and the ligands so identified and produced." (Col. 5, line 60 through Col. 6, line 6). Gold goes on to say that included in the invention is an improved method of performing PCR (Col. 6).

Gold et al. do not teach providing a first and second primer which hybridize at or near the 3' termini, or preparing cDNA from mRNA.

These would have been obvious, however, to one of ordinary skill in the art at the time of the invention. This is because providing primers which hybridize at the 3' termini, as well as preparing cDNA from mRNA, are both well known in the art and are standard procedures for synthesizing/amplifying nucleic acids. Gold et al. teach the use

of PCR, and these were both well known components of PCR at the time of the invention.

5. Claims 75-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al. in view of Langmore et al. (USPN 6,117,634).

Claim 75 is drawn to a method for sequencing a nucleic acid molecule comprising: mixing at least one nucleic acid molecule to be synthesized with one or more nucleic acid inhibitors, one or more enzymes having polymerase activity, and one or more terminating agents; incubating said mixture under conditions sufficient to synthesize a population of molecules complementary to all or a portion of said molecules to be sequenced. Claim 76 is drawn to the method of claim 75, wherein said mixing is accomplished under conditions to prevent nucleic acid synthesis and/or to allow binding of said nucleic acid inhibitor to said enzyme with polymerase activity. Claim 77 is drawn to the method of claim 75, wherein said synthesis is accomplished under conditions sufficient to denature said nucleic acid inhibitor. Claim 78 is drawn to the synthesis being accomplished in the presence of at least one component selected from nucleotides or primers. Claim 79 is drawn to the template being double stranded.

Gold et al. teach "The present invention includes methods of identifying and producing nucleic acid ligands to DNA polymerases. Specifically included are methods for identifying nucleic acid ligands to thermostable DNA polymerases useful in the Polymerase Chain Reaction, including the Taq and Tth polymerases and the nucleic acid ligands so identified and produced. More particularly, *DNA sequences are provided that are capable of binding specifically to the Taq and Tth polymerases respectively,*

thereby inhibiting their ability to catalyze the synthesis of DNA at ambient temperatures.

The method of this invention can be extended to identifying and producing nucleic acid ligands to any thermostable DNA polymerase and the ligands so identified and produced." (Col. 5, line 60 through Col. 6, line 6). Gold goes on to say that included in the invention is an improved method of performing PCR (Col. 6).

Gold et al. do not teach sequencing.

Langmore et al teach "In one embodiment, the present invention contemplates a method for sequencing nucleic acid, comprising: a) providing: i) nucleic acid template capable of being double-stranded, ii) a polymerase having a polymerase activity and a 5'-3' exonuclease activity, iv) a nucleic acid precursor, and iii) a terminating agent; b) mixing said polymerase, said precursors, said terminating agents and said template to create a reaction under conditions where said template is substantially double-stranded; and c) detecting product of said reaction under conditions whereby the nucleic acid sequence of at least a portion of said template is revealed. In one embodiment said template capable of being double-stranded comprises single-stranded nucleic acid that, upon cooling becomes substantially double-stranded." (Col. 4, lines 1-15).

It would have been obvious to one of ordinary skill in the art at the time of the invention that sequencing would have been an obvious variation on the amplification/synthesis reactions carried out by Gold. This is because it was well known in the art at the time of the invention that sequencing necessitated the same basic steps as amplification by PCR, and necessitated a polymerase whose activity would have

been inhibited by the inhibitor of the present method. For this reason, it would have been obvious to carry out a sequencing method using the inhibitor of Gold.

Summary

6. 12-29, 32-34, and 60-63, as well as 83-88 are withdrawn from consideration. Claims 64-74 are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al. (USPN 6,020,130). Claims 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al. Claims 75-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al. in view of Langmore et al. No claims are free of the prior art.

Response to Arguments

7. Applicant's arguments filed 8/18/2001 have been fully considered but they are not persuasive. Applicant has argued that the claim rejections are inappropriate because "the nucleic acid inhibitors disclosed in Gold are composed of dNTs...[and Gold] does not mention hybrid dNT-rNT inhibitor nucleic acid". The claims which are now pending, however, claims 64-82, do not recite this limitation, and the argument is therefore considered moot.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janell Taylor Cleveland, whose telephone number is (703) 305-0273.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (703) 308-1152.

Any inquiries of a general nature relating to this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1634 via the PTO Fax Center using (703) 305-3014 or 305-4227. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Janell Taylor Cleveland

October 16, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600